

May 5, 1958

Dr. Eugene Isaac Altescu  
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Dear Dr. Altescu:

Thank you for your letter of March 25.

First I must point out that you do an injustice to the venerable University of Cambridge: Hinshelwood is at Oxford.

Your experiment is an interesting one, but I fear that an opposite result would not have been very good evidence for directed progressive adaptation. It would be perfectly possible for a spontaneous resistant mutant or series of mutants to be selected from the large intermediate populations which are permitted by lower concentrations of the drugs. Your remarks about replica plating are interesting, as they are justified by the misuse made by Lam and Sevag (Jour. Bacteriology 69:184, 1955), later aptly criticized by Goldstein et al. (ibid, 70, 620, 1955). But the point I want to stress is not the technical aspects of replica plating but its use in indirect selection; which shows beyond any possibility of doubt that resistant mutants do occur spontaneously. On the other hand every observation reported by Hinshelwood & Co. can be explained by the mutation-selection hypothesis. I suggest you consult the recently published CIBA Symposium "Mechanisms of Development of drug-resistance in microorganisms" for the most up to date discussion.

I am also sending a reprint of a recent paper on indirect selection (Genetics, May 1956) by separate cover.

Yours sincerely,

Joshua Lederberg  
Professor of Medical Genetics

JL/ew